

**201-15003A**

**4-Nonanone, 2,6,8-Trimethyl-  
(Isobutyl Heptyl Ketone; IBHK; CAS RN 123-18-2)  
High Production Volume (HPV) Chemical  
Challenge Test Plan and Data Review**

Prepared for:

**The Dow Chemical Company**

Prepared by:

**Toxicology/Regulatory Services, Inc.**

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## Test Plan

4-Nonanone, 2,6,8-Trimethyl- (Isobutyl Heptyl Ketone; CAS RN: 123-18-2)		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	Testing Required
STUDY		Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
PHYSICAL AND CHEMICAL DATA								
2.1	Melting Point	Y	N	N	Y	N	Y	N
2.2	Boiling Point	Y	N	N	Y	N	Y	N
2.4	Vapor Pressure	Y	N	N	Y	N	Y	N
2.5	Partition Coefficient	Y	N	N	N	Y	Y	N
2.6	Water Solubility	Y	N	Y	Y	N	Y	N
ENVIRONMENTAL FATE AND PATHWAY								
3.1.1	Photodegradation	Y	N	N	N	Y	Y	N
3.1.2	Stability in Water	Y	N	N	Y	N	Y	N
3.3	Transport and Distribution	Y	N	N	N	Y	Y	N
3.5	Biodegradation	N	N	N	N	N	N	Y
ECOTOXICITY								
4.1	Acute Toxicity to Fish	N	N	N	N	N	N	Y
4.2	Toxicity to Daphnia	N	N	N	N	N	N	Y
4.3	Acute Toxicity to Algae	N	N	N	N	N	N	Y
TOXICITY								
5.1	Acute Toxicity	Y	N	N	Y	N	Y	N
5.4	Repeated Dose Toxicity	N	N	N	N	N	N	Y
5.5	Genotoxicity <i>In Vitro</i> (Bacterial Test)	N	N	N	N	N	N	Y
5.5	Genotoxicity <i>In Vitro</i> (Mammalian Cells)	N	N	N	N	N	N	Y
5.8.	Reproductive Toxicity	N	N	N	N	N	N	Y
5.9	Development Toxicity / Teratogenicity	N	N	N	N	N	N	Y

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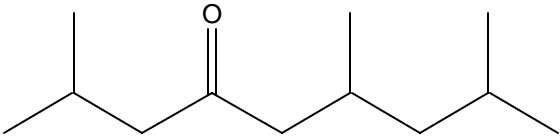
**1.0 Introduction**

This document provides a Test Plan and reviews the data availability for the High Production Volume (HPV) Chemical Challenge endpoints for 4-Nonanone, 2,6,8-trimethyl-, hereafter called Isobutyl Heptyl ketone [IBHK; CAS RN 123-18-2]. IBHK is sponsored by The Dow Chemical Company.

**2.0 General Use and Exposure**

Isobutyl Heptyl Ketone is a high molecular weight ketone produced exclusively by The Dow Chemical Company and marketed under the trade name ECOSOFT™ Solvent IK. It is used as an intermediate to make an extraction solvent for mining and in the production of 2,6,8-trimethyl-4-nonanol. During 2002, between 1 and 3 million pounds were produced either for sale to the mining industry or to be hydrogenated into an alcohol for internal use. Because of its excellent solvent properties, isobutyl heptyl ketone can be used in industrial cleaners and degreasers, and with the trend toward low volatility solvents with strong solvency, it may find additional uses in coating applications.

**3.0 General Substance Information (Identity)**

Chemical Name	4-Nonanone, 2,6,8-Trimethyl-
Synonyms	Isobutyl Heptyl Ketone (IBHK) 2,6,8-Trimethyl-4-nonanone 2,6,8-Trimethylnonan-4-one
CAS Number	123-18-2
Structure	
Molecular Weight	184.32
Substance Type	Organic
Physical State	Liquid
Odor	Obnoxious
Purity	2,6,8-Trimethyl-4-nonanone (CAS 123-18-2) >=95%; <=100% 4-Nonanol, 2,6,8-trimethyl- (CAS 123-17-1) <= 4%

#### **4.0 Physical/Chemical Properties**

A data summary for IBHK is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

##### **4.1 Melting Point**

The melting point for IBHK is listed as  $-75.2^{\circ}\text{C}$  (DIPPR, 2000). This value is considered adequate to meet the HPV Chemical Challenge requirements.

##### **4.2 Boiling Point**

The boiling point for IBHK is listed as  $218.3^{\circ}\text{C}$  (DIPPR, 2000). This value is considered adequate to meet the HPV Chemical Challenge requirements.

##### **4.3 Vapor Pressure**

The vapor pressure for IBHK is listed as 0.074 hPa at  $20^{\circ}\text{C}$  (DIPPR, 2000). This value is considered adequate to meet the HPV Chemical Challenge requirements.

##### **4.4 Partition Coefficient**

The log  $K_{ow}$  for IBHK is predicted by EPIWIN to be 3.96 (U.S. EPA, 2000a). This value is consistent with the known properties of IBHK and is considered adequate to meet the HPV Chemical Challenge requirements.

##### **4.5 Water Solubility**

The water solubility value for IBHK was determined using an ASTM method to be 22 mg/L (Wilson, 2000). Therefore, IBHK is only slightly soluble in water. This value is considered adequate to meet the HPV Chemical Challenge requirements.

#### **5.0 Environmental Fate**

A data summary for IBHK is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

##### **5.1 Photodegradation**

The model prediction for atmospheric photodegradation provides a second order rate of reaction with hydroxyl radicals of  $23.2 \text{ E-}12 \text{ cm}^3/\text{molecule-sec}$  and a  $t_{1/2}$  of 5.5 hours (U.S. EPA, 2000b). The vapor pressure of IBHK (0.074 hPa) is low and significant quantities would not be expected in the atmosphere. Degradation of any accidental release would be anticipated based on the model prediction. These data are considered adequate to meet the HPV Chemical Challenge requirements.

##### **5.2 Stability in Water**

IBHK does not react with water; the only functionality other than carbon-carbon and carbon-hydrogen bonds is the carbonyl group which does not hydrolyze.

### 5.3 Transport and Distribution

The Level III fugacity model (U.S. EPA, 2000c) was used to predict the distribution of IBHK released into the environment. Environmental exposure to IBHK is limited based on the use patterns as an industrial intermediate and solvent. For example, IBHK is not listed on the Toxic Release Inventory. Therefore, only accidental releases were considered for the fugacity modeling. Two scenarios, 100% release to air and 100% release to water were examined. For the air release the model predicted a distribution of 96% into atmosphere, 3% into water, 1% into soil, and < 1% into sediment. For the water release, the model predicted a distribution of 2% into atmosphere, 92% into water, < 0.1% into soil, and 6% into sediment. These data are considered adequate to meet the HPV Chemical Challenge requirements.

### 5.4 Biodegradability

No data were identified for the biodegradability of IBHK. A biodegradation study for IBHK according to OECD Guideline 301D will be conducted.

## 6.0 Ecotoxicity

A data summary for IBHK is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

### 6.1 Toxicity to Fish

No data were identified for the acute toxicity to fish for IBHK. An acute toxicity study with *Pimephales promelas* according to OECD Guideline 203 will be conducted.

### 6.2 Toxicity to Aquatic Invertebrates

No data were identified for toxicity to aquatic invertebrates for IBHK. An acute toxicity study with *Daphnia magna* according to OECD Guideline 202 is in progress.

### 6.3 Toxicity to Aquatic Plants

No data were identified for toxicity of IBHK to aquatic plants. An acute toxicity study with the algae, *Selenastrum capricornutum*, according to OECD Guideline 201 is in progress.

## 7.0 Human Health-Related Data

A data summary for IBHK is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

### 7.1 Acute Toxicity

The following acute toxicity data are available: acute oral LD<sub>50</sub> in rats = 8470 mg/kg bw; acute dermal LD<sub>50</sub> in rabbits = 9030 mg/kg bw; 2 of 6 rats died after an 8-hr exposure to substantially saturated vapor; and 6 of 6 rats died when exposed to the test substance as a cooled mist for one hour (Carpenter, 1948). These data are considered adequate to meet the HPV Chemical Challenge requirements.

## 7.2 Repeated Dose Toxicity

No data were identified for repeated dose toxicity. An oral (gavage) study according to OECD Guideline 422 is in progress.

## 7.3 Genetic Toxicity (*in vitro*)

No data were identified for *in vitro* mutagenicity screening. A bacterial reverse mutation assay study according to OECD Guideline 471 and a chromosomal aberration study according to OECD Guideline 473 are in progress.

## 7.4 Reproductive and Developmental Toxicity

No data were identified for reproductive or developmental toxicity. An oral (gavage) study according to OECD Guideline 422 is in progress.

# 8.0 Conclusion

Adequate information is available for melting point, boiling point, vapor pressure and water solubility of IBHK. Partition coefficient, photodegradation and environmental distributions are adequately supported by the appropriate model data. IBHK does not have hydrolyzable groups and is stable in abiotic aqueous systems. IBHK is relatively non-toxic following acute oral and dermal exposure. Inhalation exposure may result in toxicity to the lung although significant exposure is not anticipated based on the low vapor pressure and the obnoxious odor of IBHK. The following additional testing is scheduled or in progress: biodegradation (OECD 301D); acute aquatic toxicity to fish, invertebrates, and algae (OECD 203, 202 and 201, respectively); a repeated dose, reproductive and developmental screening study via gavage according to the OECD Guideline 422 protocol, and *in vitro* mutagenicity screening according to OECD Guidelines 471 (bacterial reverse mutation) and 473 (chromosomal aberrations in mammalian cells). The available data and the studies in progress or scheduled to be conducted are considered adequate to meet the HPV Chemical Challenge Program requirements.



## **9.0 References**

Carpenter, C.P. 1948. The Acute Toxicity of Trimethyl Nonanone. Unpublished Report Number 11-90. Mellon Institute of Industrial Research, University of Pittsburgh, PA, USA.

DIPPR (The Design Institute for Physical Properties). 2000. The DIPPR Information and Data Evaluation Manager, Version 1.5.0, Copyright BYU-TPL2000.

U.S. EPA (U.S. Environmental Protection Agency). 2000a. EPI Suite™, Version 3.11; KOWWIN Program, Version 1.67; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

U.S. EPA (U.S. Environmental Protection Agency). 2000b. EPI Suite™, Version 3.11; AOPWIN Program, Version 1.91; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

U.S. EPA (U.S. Environmental Protection Agency). 2000c. EPI Suite™, Version 3.11; Level III Fugacity Model; PC-Computer software developed by EPA's Office of Pollution Prevention Toxics and Syracuse Research Corporation (SRC).

Wilson, L.C. 2000. Liquid-Liquid Equilibrium Measurements for Eighteen Glycol Ethers, Ketones, Esters and Alcohols with Water. Project Report No. 44662, 10/13/2000. Union Carbide Corporation, S. Charleston, WV, USA.

**Table 1: HPV Data Summary**

4-Nonanone, 2,6,8-Trimethyl-  
(Isobutyl Heptyl Ketone; IBHK)

CAS NO: 123-18-2		SPECIES	PROTOCOL	RESULTS
<b>PHYSICAL-CHEMICAL</b>				
2.1	Melting Point		Handbook Data (DIPPR)	-75.2 °C
2.2	Boiling Point		Handbook Data (DIPPR)	218.3 °C
2.3	Density		Handbook Data (DIPPR)	0.818 g/cm <sup>3</sup> (at 20 °C )
2.4	Vapor Pressure		Handbook Data (DIPPR)	0.07413 hPa (at 20 °C )
2.5	Partition Coefficient (log K <sub>ow</sub> )		KOWWIN v 1.67	3.96
2.6	Water Solubility		ASTM E 1148	22 mg/L
2.7	Flash Point		Handbook Data (DIPPR)	82.9 °C
<b>ENVIRONMENTAL FATE AND PATHWAY</b>				
3.1.1	Photodegradation		AOPWIN v 1.91	half-life: 5.5 hours (OH Rate Constant)
3.1.2	Stability in Water		Hydrolysis @ 25 °C	Does not react with water; the only functionality other than carbon-carbon and carbon-hydrogen bonds is the carbonyl group which does not hydrolyze
3.3	Transport and Distribution		Mackay Level III 100% release to air	96% into atmosphere, 3% into water, 1% into soil, < 1% into sediment
			Mackay Level III 100% release to water	2% into atmosphere, 92% into water, < 0.1% into soil, 6% into sediment
3.5	Biodegradation		OECD 301D	Study in progress
<b>ECOTOXICOLOGY</b>				
4.1	Acute/Prolonged Toxicity to Fish	<i>Pimephales promelas</i>	OECD 203	Study to be conducted
4.2	Acute Toxicity to Aquatic Invertebrates	<i>Daphnia magna</i>	OECD 202	Study in progress
4.3	Toxicity to Aquatic Plants e.g. Algae	<i>Selenastrum capricornutum</i>	OECD 201	Study in progress

**Table 1: HPV Data Summary**

4-Nonanone, 2,6,8-Trimethyl-  
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CAS NO: 123-18-2		SPECIES	PROTOCOL	RESULTS
<b>TOXICOLOGY</b>				
5.1.1	Acute Oral Toxicity	Rat	Not specified	LD <sub>50</sub> : 8470 mg/kg bw
5.1.2	Acute Inhalation Toxicity	Rat	Saturated vapor	2/6 dead @ 8 hr.
		Rat	Cooled mist	6/6 dead @ 1 hr
5.1.3	Acute Dermal Toxicity	Rabbit	Not specified	LD <sub>50</sub> : 9030 mg/kg bw
5.4	Repeated Dose Toxicity	Rat	OECD 422	Study in progress
5.5	Genetic Toxicity <i>In Vitro</i>			
	Bacterial Test (Gene mutation)	<i>Salmonella typhimurium</i>	OECD 471	Study in progress
	Chromosomal aberration	CHO	OECD 473	Study in progress
5.8	Toxicity to Reproduction / Impairment of Fertility	Rat	OECD 422	Study in progress
5.9	Developmental Toxicity / Teratogenicity	Rat	OECD 422	Study in progress